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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,972	02/18/2005	Christel Renate Schopfer	13173-00007-US	1455
23416 7590 08/27/2007 CONNOLLY BOVE LODGE & HUTZ, LLP P O BOX 2207 WILMINGTON, DE 19899			EXAMINER KALLIS, RUSSELL	
			ART UNIT 1638	PAPER NUMBER
			MAIL DATE 08/27/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/524,972

Applicant(s)

SCHOPFER ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-100 is/are pending in the application.
- 4a) Of the above claim(s) 10, 11 and 36-59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 12-35, 60-78 and 80-100 is/are rejected.
- 7) ☒ Claim(s) 79 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 February 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-100 drawn to group i) SEQ ID NO: 1 and 2; and Groups A, B O and S in the reply filed on 5/21/2007 is acknowledged.

Claims 1-100 are pending. Claims 10-11 and 36-59 are withdrawn as being drawn to non-elected inventions. Claims 1-9, 12-35 and 60-100 are examined.

Specification/Drawings

The specification does not contain a brief description of the drawings. Further, Figures 3 and 4 recite nucleotide sequences and neither the specification or the figures identify those sequences using sequence identifiers either.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9, 12-35, 60-78 and 80-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mann V. et al. Biotechnology; August 2000, Vol. 18 pages 888-892 in view Shewmaker C. WO 99/07867 published 18 February 1999 and in further view of U.S Patent application publication 2004/0176570 filed April 10, 2002, Sandmann, G. *et al.* Archives of Biochemistry and Biophysics: Minireview; Jan. 1, 2001; Vol. 385, No. 1, and Applicant's admissions of the prior art in the specification.

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The claims are broadly drawn to a method of producing ketocarotenoids in plants transformed with a ketolase and further transformed with a hydroxylase and beta-cyclase; a HMG-CoA reductase and hydroxymethylbutyl enyl diphosphate reductase; an antisense hydroxylase, and an antisense epsilon cyclase; and plants transformed thereby.

Mann teaches expression of GUS in tobacco petal tissue using the tomato PDS promoter that expresses in flower petals (page 889 in column 1 and Table 1); metabolic engineering of astaxanthin production in the nectaries of tobacco petals using a chimeric gene construct comprising the tomato *PDS* promoter fragment of bases 1-459, the transit peptide encoding sequence that imports proteins into chromoplasts, and the coding sequence for the *CrtO* β -carotene ketolase polypeptide isolated from the alga *Haematococcus pluvialis*, i.e. SEQ ID NO: 1 (page 890 in column 1, and Figure 3 and Table 2); increases of both astaxanthin and canthaxanthin in transgenic tobacco nectaries expressing the chimeric gene construct comprising the tomato *PDS* promoter fragment of bases 1-459, the transit peptide encoding sequence that imports proteins into chromoplasts, and the coding sequence for the *CrtO* polypeptide isolated from the alga *Haematococcus pluvialis* (page 890 see Table 2); and states that the production of astaxanthin in the carotenoid flower petals of marigolds is an attractive source for the commercial production of astaxanthin, a keto-carotenoid (page 890 column 2 last paragraph to page 891 line 2).

Mann does not teach further transformation with a hydroxylase and beta-cyclase; a HMG-CoA reductase and hydroxymethylbutyl enyl diphosphate reductase; an antisense hydroxylase, and an antisense epsilon cyclase.

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Shewmaker teaches manipulation of the carotenoid pathway in a plant by transformation with beta carotene hydroxylase and a keto introducing enzyme such as *crtO* is useful for the production of astaxanthin as well as increasing beta-cyclase expression on page 13 lines 24 to page 14 line 1; and antisense inhibition of lycopene epsilon cyclase to increase flux of beta-carotene for the production of astaxanthin; or the combination of the ketolase *crtO* and antisense of beta hydroxylase to produce canthaxanthin i.e. a ketocarotenoid in figure 8 (see page 13 lines 4-25 to page 14 line 14; especially page 13 lines 4-9, 19-22, 26-28; and page 14 line 1, and lines 2-3; and figure 8 and page 1 of patent).

U.S Patent application publication 2004/0176570 teaches hydroxymethylbutyl enyl diphosphate reductase is useful for the production of carotenoid and isoprenoid precursors in transformed plants on page 3 column 1; in figure 2 and claims 15-16; and in claims 76-77 and page 11 column 1.

Sandmann teaches increased carotenoid formation in yeast transformed with HMGCoA reductase catalytic region on page 10 column 1 last seven lines of the 2nd full paragraph and part A of figure 2 on page 6.

Applicant's specification teaches that the claimed sequences were taught in the art see page 6 (ketolase SEQ ID NO: 1-2); page 18 (hydroxylase SEQ ID NO: 17-18 and beta cyclase SEQ ID NO: 19-20); page 60 (HMG-CoA reductase SEQ ID NO: 99-100); page 61 (hydroxymethylbutyl enyl diphosphate reductase SEQ ID NO: 101-102); SEQ ID NO: 38 in Example 12 as GenBank Accession AF251016, including the promoter portion of SEQ ID NO: 47 comprised in SEQ ID NO: 38 Gen Bank Accession AF251016:

It would have been obvious at the time of invention to modify the invention of Mann, using the *crtO* gene, to also include increased beta carotene hydroxylase and beta cyclase expression along with antisense of lycopene epsilon cyclase as taught by Shewmaker to increase flux to beta carotene production for increased production of ketocarotenoids i.e. astaxanthin; . One of ordinary skill in the art would have been motivated by the knowledge that ketolase encoding polynucleotides are valuable materials for producing recombinant astaxanthin and canthaxanthin in transformed plants as taught by Mann and Shewmaker, that production of astaxanthin and canthaxanthin in petals of transgenic plants was possible as taught by Mann's teaching of petal specific expression of *GUS* using the tomato *PDS* promoter and chromoplast transit peptide, that heterologous expression of the *CrtO* gene and production of astaxanthin and canthaxanthin in tobacco floral nectaries using a construct comprising the tomato *PDS* promoter and chromoplast transit peptide fused to the *CrtO* gene would apply to the commercially attractive plant Marigold as taught by Mann, and that antisense of genes encoding lycopene epsilon cyclase would further enhance as taught by Shewmaker; that expression of upstream isoprenoid precursor pathway genes encoding DHR and HMG-CoA reductase would also further enhance ketocarotenoid biosynthesis in plant flower petals by increasing flux of isoprenoid precursors toward production of beta-carotene as taught by Sandmann and U.S Patent application publication 2004/0176570 and that one would have had a reasonable expectation of success of producing astaxanthin and canthaxanthin in the flower petals of transformed plants given the success of Mann in directing expression of *GUS* into the petals of tobacco using the tomato *PDS* promoter and chromoplast transit peptide and in producing astaxanthin and canthaxanthin in the floral nectarines of tobacco transformed with the *crtO* gene, and by the knowledge that the

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chromoplasts found in the petals of marigold have commercial levels of carotenoid substrate for producing the ketocarotenoids astaxanthin and canthaxanthin; and wherein making double stranded sense-antisense RNA from promoter sequences or coding sequences is obvious given the lack of criticality.

Claims are rejected.

Claim 79 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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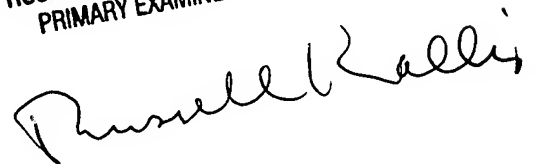
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Russell Kallis Ph.D.
August 10, 2007

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER

A handwritten signature in cursive script that reads "Russell Kallis".